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EXAMINER	
FOSTER, CHRISTINE E	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,006	KARL ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-52 and 70-72* is/are pending in the application.

4a) Of the above claim(s) *70-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ~~5/21/04~~.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Please note that the examiner in this application has changed. The new examiner, Christine Foster, can be reached at (571) 272-8786.

Response to Amendment

Applicant's amendments, filed 5/17/05, are acknowledged and have been entered. Applicant's addition of claims 70-72 is acknowledged and has been entered. Claims 44-52 and 70-72 are currently pending. Claims 70-72 are withdrawn from consideration as being drawn to non-elected inventions (see below).

Rejections Withdrawn

Applicant's amendments are persuasive to overcome the rejection of claims 44 and 45 under 35 USC 102 (Bellet et al.). Applicant's amendments are persuasive to overcome the rejection of claims 46-48 under 35 USC 103 (Bellet et al. in view of Kuo). However, the amended claims present new grounds for rejection as detailed below.

Election/Restrictions

Newly submitted claims 70-72 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 70-72 are directed to a method for detection by measuring at least two agent-specific antigens, at least two agent-specific antibodies, or at least one agent-specific antigen and one agent-specific antibody. The method includes the steps of contacting the sample with a detection reagent comprising one or more receptors which bind specifically with at least two agent-specific components and of determining the presence of amount of a signal-generating group via a component-specific cut-

off, which are not limitations of the method of claims 44-48. The method of claims 44-48 includes the limitation of an analyte comprising at least two epitopes, which is not a limitation of claims 70-72. New claims 70-72 are related to claims 49-52 as product and process of use and are patentably distinct as the solid phase of claims 49-50 and the test kit of claims 51-52 may be used in either the method of claims 44-48 or in the newly presented method of claims 70-72.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 70-72 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Information Disclosure Statement

Applicant's lnformation Disclosure Statement filed 5/21/01 was received and entered into the application. The references therein have been considered by the examiner as indicated on the attached form PTO-1449.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 44-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Amended claim 44 now recites a signal generating group that is bound separately to the first and second test areas via the analyte. Support cannot be found where indicated by applicant for the limitation that the signal generating group is bound separately to the test areas.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 49 and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Bellet et al. (US Pat. 5,011,771). The reference discloses an immunometric assay comprising the formation of a complex between antigen and multiple immobilized monoclonal antibodies against different epitopes of the antigen and with a detectably labeled monoclonal antibody (abstract). The sandwich or immunometric assay is meant to include simultaneous, forward, and reverse sandwich assays (Col. 5, lines 24-30). In a forward immunometric assay, sample is contacted with solid phase bound antibodies such that antigen in the sample is bound to the solid phase bound antibodies. Detectably labeled antibodies are then added to the solid phase. Labeled antibody on the solid phase is then detected as an indication of analyte presence (Cols. 5-6). The

solid phase of the reference is an immunoabsorbent, which may be beads formed from glass, polystyrene, polypropylene, dextran, nylon, and other materials, or tubes formed or coated with such materials (Col. 8, lines 1-3). According to the reference, the multiple immobilized antibodies are bound to the same solid phase, as close proximity is important (Col. 8, lines 7-9). The monoclonal antibody may be labeled with any detectable label (Col. 8, lines 20-21). Any animal sample containing a detectable antigen can be used in the assay (Col. 8, lines 31-35). Any multivalent antigen can be detected with the assay of the reference, including viral antigens such as Hepatitis B, Herpes Simplex viruses 1 and 11, Herpes Virus Zoster, cytomegalovirus, Epstein-Barr virus, and Papova viruses such as measles, rubella, or influenza (Col. 8, lines 62-68). The materials for use in the assay are ideally suited for packaging in a kit (Col. 9, lines 62-63). In addition, the method of the reference inherently has an inert surface that does not bind analyte or other sample components located between the two immobilized antibodies, as Figures IB, IC, and ID all show separation between the two immobilized antibodies with no interaction whatsoever occurring in this area.

The instant claims recite that the solid phase and test kit are "for simultaneous separate multiepitope detection." A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. As the solid phase and test kit of Bellet et al. are capable of performing the intended use, it anticipates the instant claims.

Claims 44, 47, and 49, and 51 are rejected under 35 U.S.C. 102(e) as being anticipated by Linsley et al. (US Patent No. 6,004,761, filed June 2, 1995).

Linsley et al. teach double determinant immunoassay (DDIA) methods wherein a capture antibody is immobilized on a solid phase such as a plastic support or polystyrene microtiter plate, in order to detect an antigen present in a fluid sample (column 4, lines 6-30; column 13, lines 2-4 in particular). Following capture of the antigen by the immobilized antibody, a labeled antibody is added which may bind to a different epitope on the captured antigen than the immobilized antibody (column 4, lines 11-17 and 21-30; Examples IV, VII, and IX; and Tables 5 and 12 in particular). In particular, Linsley et al. teach immobilization of multiple antibodies that are specific for different epitopes of the mucin antigen (see in particular column 2, lines 56-63; column 17, lines 21-23; and columns 24 to column 25, line 44), wherein each type of antibody is bound to a spatially separate test area, i.e. a different well of a microtiter plate (column 17, lines 57-60 in particular). It is apparent to one of skill in the art that microtiter plates comprise an inert surface between the wells that does not bind to the analyte or other sample components. The sample (diluted sera, control or standard) is contacted with the solid phase and with a detection reagent comprising a third receptor (W1-HRP conjugated antibody) that binds with the antigen (see column 2, lines 10-11) and that is bound to a signal generating group (HRP), and the presence of amount of the signal generating group is determined for each well in order to determine the amount of antigen in the sample (see column 18, lines 18-41; Table 5; column 19, lines 14-26; and column 25, lines 46-64; and column 4, lines 15-18 in particular).

With regard to claim 47, serum from a patient without cancer is added to some of the wells as a control (column 4, lines 10-11; column 17, line 65 to column 18, line 19).

With regard to claim 51, Linsley et al. teach diagnostic test kits for detection of mucin antigens in serum or other specimens via the DDIA method (column 30, line 55 to column 31, line 32).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 50 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bellet et al. (US Pat. 5,011,771) in view of Kuo (EP 0 813 064).

Bellet et al. teach a multiepitopic assay, as previously discussed under 35 USC 102(b). However, the reference does not teach the diameter of the test area, a control area, or latex particles as the label.

Kuo teaches a solid support on which an antibody specific to an epitope of an analyte and a first labeled antibody, which is specific to another epitope of the analyte, are immobilized. A second labeled antibody is also provided which is specific to the first labeled antibody (abstract). The signal generated by the complex is detected on the substrate. The solid support of the reference may be any of those materials known in the art as being suitable for conducting immunoassays, such as the interior surface of a microtiter well (Col. 3). According to one embodiment, there is a reagent region containing a second antibody labeled with gold sol, a second reagent region containing a third antibody labeled with gold sol, and a capture zone with immobilized first antibody (Col. 4). Although the regions may overlap, it is not necessary and there may be spacing between the regions (Cols. 4-5). The support may also be provided with a positive control zone (Col. 5). Metal sols are the preferred signal generators, but any species producing a detectable signal may be used, including latex particles (Col. 5).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the control area and latex particles as the label of Kuo with the method and kit of Bellet et al. because the use of a control area allows determination of background or baseline, which permits calibration of the assay system and a more sensitive measurement of analyte presence. In addition, since Bellet et al. teach that any suitable label may be used with

their method, one could have used latex particles with a reasonable expectation of success. Further, the selection of a specific label simple represents an optimization of the assay protocol that one of skill in the art could have easily chosen based on preference. It has been held to be within the general skill of a worker in the art to select a known material on the basis of its suitability for the intended use as a matter of obvious design choice. *In re Leshin*, 125 USPQ 416. It would also have been obvious to use test areas with diameters less than 1 mm. Bellet et al. teach that immobilized antibodies must be in close proximity to each other, and choosing the actual size of the area simply represents an optimization of the assay. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Claim 45-46 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Linsley et al. in view of Mehta et al. (US Patent No. 5,173,399).

Linsley et al. is as discussed above, which fails to teach a method wherein the analyte detected is selected from the group consisting of HIV I, HIV II, HBV and HCV-antibodies and HIV antigens.

Mehta et al. teach several monoclonal antibodies that recognize at least three different epitopes on HIV-1 p24 antigen, which may be used in a diagnostic test to detect HIV-1 p24 in biological fluids (the abstract; column 2, lines 17-46; and column 12, lines 18-43 in particular).

Therefore, it would have been obvious to one of skill in the art to employ the monoclonal antibodies taught by Mehta et al. in a method for detecting a multiepitope-bearing antigen, such as the method of Linsley et al., in order to detect HIV-1 p24. One would have had reasonable

expectation of success because Mehta et al. teach that the p24 antibodies are suitable for use in a diagnostic immunoassay employing capture antibodies.

With regard to claims 46 and 50, it would have been obvious to use test areas with diameters less than 1 mm as Linsley et al. teach that the antibodies may be immobilized on a plastic support or column, and choosing the actual size of the area simply represents an optimization of the assay. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Claims 46, 48, 50 and 52 rejected under 35 U.S.C. 103(a) as being unpatentable over Linsley et al. in view of Valkirs et al. (US Patent No. 6,348,318).

Linsley et al. teach examples of detection reagents that comprise radionuclides such as ^{125}I or the enzyme HRP (see column 4, lines 11-15), but fail to specifically teach a detection reagent comprising labeled latex particles.

Valkirs et al. teach detection reagents comprising suitable detection labels, which may be HRP or may be colorimetric labels such as latex beads (column 11, lines 13-34), for use in detection of target analytes.

Therefore, it would have been obvious to one of ordinary skill in the art to substitute colorimetric latex beads as taught by Valkirs et al. for the HRP label in the method of Linsley et al. because Valkirs et al. teach that both HRP and latex beads are suitable detection labels for detection of analytes using labeled antibody detection moieties. One would have had reasonable expectation of success because Valkirs et al. teach that such labels are suited for use with antibody detection moieties, which are also components of the detection reagents of Linsley et al.

Response to Arguments

Applicant's amendments and arguments filed 5/27/05 have been fully considered. The amendment of claim 44 is persuasive to overcome the rejection of claims 44-45 under 35 USC 102 (Bellet et al.) and of claims 46-48 under 35 USC 103 (Bellet et al. in view of Kuo), as Bellet et al. teaches a signal generating group that is bound to the first and second test areas via the analyte, but fails to teach a method wherein the signal generating group is bound separately to the first and second test areas via the analyte, as recited in lines 14-15 of the amended claim.

Applicant indicates that claim 44 has been amended to explicitly indicate that the method requires that each test area be separately assayed for the signal generating group for the detection of the analyte in each separate test area (see "Remarks" p. 5). Applicant further argues that the claims are not anticipated by Bellet et al. because Bellet does not teach separate detection of the analyte in each of the test areas (Remarks p. 6). This argument is moot in light of the withdrawal of the rejection of claims 44-45 and 46-48. However, it is noted for the record that the examiner disagrees that the amended claim reflects the limitation of separate detection of the analyte in each of the test areas. Applicant has amended claim 44 to recite:

> (c) determining presence or amount of the signal generating group bound separately to the first and second test areas via the analyte as a measure of the analyte in said sample

The new limitation does not recite that each test area is separately assayed; rather, the placement of the word "separately" in the claim indicates that the signal generating group is separately bound, which appears to represent a departure from the specification and claims as originally filed (see 112, 2nd paragraph rejection above).

Applicant's amendments and arguments are not persuasive to overcome the rejections of claims 49 and 51 under 35 USC 102 and of claims 50 and 52 under 35 USC 103. In response to applicant's argument that amended claims 49 and 51 now explicitly require that the solid phase and test kit are for simultaneous separate multiepitope detection, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Applicant has argued that the claims are not anticipated by Bellet et al. because Bellet et al. do not teach a test area containing only one type of analyte-specific receptor and a non-porous support with first and second spatially separate test areas (Remarks p. 6, last paragraph). The examiner disagrees because the two immobilized antibodies of Bellet appear to define spatially separate test areas separated as shown in Figures 1B, 1C and 1D as noted above under 35 USC 102. Because each immobilized antibody defines a test area, each test area contains only one type of analyte-specific receptor. Furthermore, Bellet et al. do in fact teach non-porous supports as discussed above under 35 USC 102.

Applicant has also argued that the claims are not anticipated by Bellet et al. because Bellet et al. do not teach separate detection of the analyte in each of the test areas (Remarks p. 6, last paragraph). Applicant further argues that the Office has not shown that all of the claim limitations are taught in or obvious from the prior art because Bellet et al. and Kuo fail to teach separate assays (p. 9). However, separate detection and/or assay is not a limitation of claims 49-52.

Furthermore, with regard to Applicant's argument that claims 49 and 51 require simultaneous separate testing of the first and second test areas, the recitation of "simultaneous separate multiepitope detection" in the claims has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

The following is also cited by the examiner as prior art of relevance:

Ekins (US Patent No. 5,837,551) teaches methods for detection of analytes in which binding agents such as antibodies are immobilized on a solid support as microspots.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached at (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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